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## WHAT IS CLAIMED IS:

- 1. A method for identifying a peptide-peptide interaction comprising:
  - (a) providing a first fusion construct comprising target peptide fused to a first DNA binding domain;
  - (b) providing a second fusion construct comprising a library encoded peptide (LEP) fused to second DNA binding domain (DBD), wherein said second DBD works as a complex with said first DBD to facilitate binding of said complex to a prokaryotic operator region;
  - (c) contacting said first and second fusion constructs in a prokaryotic host cell which comprises said prokaryotic operator region, wherein said prokaryotic operator region is operationally linked to a coding region for one or more indicator polypeptides; and
  - (d) determining binding of said complex to said operator region,
    whereby binding of said complex to said operator region identifies said LEP as a
    binding partner for said target peptide.
- 2. The method of claim 1, wherein binding of said complex to said operator acts blocks the transcription of said coding region.
- 3. The method of claim 1, wherein said one or more indicator polypeptides render said prokaryotic host cell insensitive to phage infection.
  - 4. The method of claim 3, wherein step (d) comprises infection with a phage that infects, replicates and lyses said prokaryotic host cell.
  - 5. The method of claim 4, wherein said operator is the lacZ operator, and the first and second DBDs are derived from the  $\lambda$  repressor.

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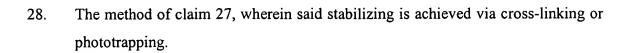
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- 6. The method of claim 1, wherein one or more indicator polypeptides produce a colorimetric or fluorescent product.
- 7. The method of claim 1, wherein said one or more indicator polypeptides is  $\beta$ -gal.
- 8. The method of claim 1, wherein said target peptide is 5 to about 5000 residues in length.
  - 9. The method of claim 1, wherein said target peptide is 10 to about 2000 residues in length.
  - 10. The method of claim 1, wherein said LEP is 5 to about 50 residues.
  - 11. The method of claim 1, wherein said first and second fusion constructs are encoded by a nucleic acid segment under the control of a promoter operable in said prokaryotic host cell.
  - 12. The method of claim 1, wherein said target peptide and LEP bind with an affinity in the range of about 10<sup>-3</sup> to about 10<sup>-6</sup> M.
  - 13. The method of claim 12, wherein said target peptide and LEP bind with an affinity in the range of about 10<sup>-4</sup> M.
  - 14. The method of claim 12, wherein said target peptide and LEP bind with an affinity in the range of about 10<sup>-5</sup> M.
  - 15. The method of claim 12, wherein said target peptide and LEP bind with an affinity in the range of about 10<sup>-6</sup> M.
- 20 16. The method of claim 1, further comprising random mutagenesis of said LEP, followed by measuring the change, if any, in the binding affinity of said LEP for said target.
  - 17. The method of claim 16, wherein said measuring comprises effecting binding of said LEP to said target peptide under conditions more stringent than in claim 1.

- 18. The method of claim 1, further comprising:
  - (e) linking said identified LEP to a third peptide, whereby said linking permits said identified LEP and said third peptide to interact independently with said target peptide;
- (f) then contacting said target peptide with the identified LEP-third peptide complex, and
  - (g) followed by determining the change, if any, in the binding affinity of said LEP for said target peptide.
- 19. The method of claim 18, wherein said measuring comprises effecting binding of said LEP to said target peptide under conditions more stringent than in claim 1.
  - 20. The method of claim 18, wherein said third peptide is known to bind said target peptide.
  - 21. The method of claim 18, wherein said third peptide is a member of a peptide or peptidomimetic library.
- 15 22. The method of claim 1, wherein said target peptide is an enzyme substrate, an antigen, or a eukaryotic cell antigen.
  - 23. The method of claim 22, wherein said target peptide is an enzyme substrate.
  - 24. The method of claim 23, wherein said enzyme substrate is bacterial, viral or fungal antigen.
- 20 25. The method of claim 22, wherein said target peptide is a eukaryotic cell antigen.
  - 26. The method of claim 25, wherein said eukaryotic cell antigen is a tumor cell marker, an HLA antigen, a cell surface receptor, or a cell surface transporter.
  - 27. The method of claim 1, further comprising, prior to said determining, the step of stabilizing the interaction between said target peptide and said LEP.

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- 29. The method of claim 1, wherein said first peptide comprises a multimer of a smaller peptide unit.
- 5 30. The method of claim 1, further comprising assessing binding of said target peptide to said identified LEP by Western blot, mass spectroscopy, or nuclear magnetic resonance.

A method for screening a peptide library for peptide-peptide interactions comprising:

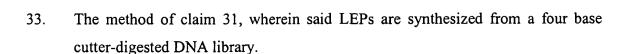
(a) providing a plurality of a first fusion construct comprising a target peptide fused to a first DNA binding domain;

(b) providing a plurality of second fusion construct comprising a library of encoded peptide (LEPs) fused to second DNA binding domain (DBD), wherein said second DBD works as a complex with said first DBD to facilitate binding of said complex to a prokaryotic operator region;

- (c) transferring said pluralities of first and second fusion constructs into a prokaryotic host cell which comprises said prokaryotic operator region, wherein said prokaryotic operator region is operationally linked to a coding region for one or more indicator polypeptides; and
- 20 (d) determining binding of complexes to said operator region,
  whereby binding of said complexes to said operator region identifies associated
  LEPs as binding partners for said target peptide.
  - 32. The method of claim 3, wherein steps (a)-(d) are repeated at least once using the LEP identified in step (d).

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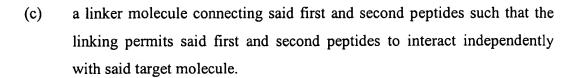


- 34. The method of claim 33, further comprising the step of sequencing a DNA encoding an identified LEP.
- 5 35. A library encoded peptide (LEP) selected according to a method comprising:
  - (a) providing a first fusion construct comprising target peptide fused to a first DNA binding domain;
  - (b) providing a second fusion construct comprising said LEP fused to second DNA binding domain (DBD), wherein said second DBD works as a complex with said first DBD to facilitate binding of said complex to a prokaryotic operator region;
  - (c) contacting said first and second fusion constructs in a prokaryotic host cell comprising said prokaryotic operator region, wherein said prokaryotic operator regions is operationally linked to a coding region for one or more indicator polypeptides; and
  - (d) determining binding of said complex to said operator region,

    whereby binding of said complex to said operator region identifies said

    LEP as a binding partner for said target peptide.
  - 36. A heterodimeric binding molecule comprising:
    - (a) a first peptide that binds to a target molecule;
      - (b) a second peptide that binds to said target molecule,

wherein at least one of said first and second peptides is a member of a peptide library; and



- 37. The binding molecule of claim 36, further comprising a moiety that permits recovery of said molecule.
- 38. The binding molecule of claim 37, wherein said moiety is a magnetic bead.
- 39. The binding molecule of claim 36, wherein said heterodimeric binding molecule is expressed on the surface of a phage.